Lithium carbonate augmentation therapy in fibromyalgia

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Fibromyalgia (fibrositis) is a disorder of unknown cause. The typical features are multiple tender points, musculoskeletal pain and stiffness, and unrestorative sleep. The formulation by Smythe and Moldofsky[1] of acceptable diagnostic criteria and the demonstration of the effectiveness of tricyclic antidepressants[2] (TCAs) have helped physicians to recognize and better manage this common disorder. The benefit of TCAs in fibromyalgia is partly understandable, given the high frequency of depression in chronic pain states.[3,4] However, the improvement may be incomplete or short-lived. In a 12-week study only 21 of 61 patients responded moderately or very well to cyclobenzaprine therapy.[5] Carette and associates[6] found that the most marked response occurred in the first 2 to 4 weeks of a 9-week double-blind trial of amitriptyline.

The combination of lithium carbonate and TCAs has been used in psychiatry since 1973.[7] Most studies of such therapy have not been controlled, but the large number of reports seems to indicate a consensus on its clinical usefulness.[8] Lithium may augment the antidepressant effect of TCAs in resistant unipolar depression.[9-12] There is strong evidence that it also prevents the emergence of mania or hypomania in patients with bipolar depression during treatment with TCAs.[7] In addition, combination therapy has been used for psychotic depression.[13] The combination of amitriptyline and lithium has been effective in treating the painful shoulder syndrome.[14]

The clinical features common to fibromyalgia, chronic pain states and the painful shoulder syndrome — depression, chronic joint pain[15] and disturbed sleep[14] — suggest that lithium is a useful adjunct to TCA therapy for fibromyalgia. I report three cases of fibromyalgia that was refractory to TCA therapy but improved markedly after the addition of lithium. Such use of lithium has not been reported previously.

Case reports

Case 1

A 48-year-old woman presented with a 22-year history of recurrent episodes of unipolar depression and a 3-year history of polymyalgia, polyarthralgia, morning stiffness, anergia and headaches. She was taking amitriptyline, 50 mg four times daily, and indomethacin, 75 mg twice daily, without appreciable pain relief.

There was a full range of movement of all the joints except the neck, and there were no inflammatory changes. Multiple fibrositic trigger points were found about the neck, the shoulders, the arms and the knees. The results of tests for rheumatoid factor and antinuclear antibody were repeatedly negative. The erythrocyte sedimentation rate and the blood urea nitrogen level were normal. Selective radiologic examination revealed early osteoarthritic changes in the cervical spine.

The indomethacin therapy was withdrawn, and treatment with lithium carbonate was started. The eventual dose was 300 mg four times daily, which resulted in a steady-state serum lithium level of 0.5 to 0.6 mmol/L. There was a dramatic reduction of stiffness, pain and easy fatigability after 3 months. Previously identified trigger points, however, were still markedly tender. The patient had no depressive symptoms during the lithium therapy.

The lithium therapy was stopped after 7

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months, when the triiodothyronine uptake was 0.34 (normally 0.35 to 0.45), the thyroxine level 92 (normally 79 to 157) nmol/L and the blood urea nitrogen level 4.0 (normally 3.0 to 8.0) mmol/L. The patient had minimal transient stiffness and pain 18 months after the lithium therapy was stopped. She was still receiving amitriptyline at the same daily dose.

Case 2

A slender, 49-year-old woman complained of pain in the neck, the shoulders, the middle and lower portions of the back, and the left knee since a motor vehicle accident 13 years before. She also had a history of severe recurrent headaches and three hospital admissions for psychiatric treatment. She had been given trimipramine, methotrimeprazine and haloperidol. At presentation for rheumatologic assessment she was still taking trimipramine, 225 mg/d, and diazepam at bedtime.

The woman appeared tense and demonstrated motor restlessness, pressured speech and bizarre posturings. There were no signs of inflammation or organic disturbance of the joints. Multiple trigger points were found in the soft tissue of the neck, back, hips and left knee. The results of radiologic examination of the lumbar spine, cervical spine and left knee were normal, as were those of laboratory investigations.

The trimipramine treatment was continued and augmentation therapy with lithium started; the dose was initially 300 mg twice daily and then was increased to 300 mg four times daily to achieve a steady serum lithium level of 0.6 mmol/L. One year later the woman reported minimal joint symptoms and many days of no pain. Her affect was unremarkable and appropriate, and there were no overt signs of agitation. The blood urea nitrogen level and the results of thyroid function studies were normal; her thyroid gland was impalpable.

Case 3

A 3-year history of diffuse muscle and joint pain as well as stiffness in the elbows, the shoulders, the left side of the lower back and the leg prompted a 56-year-old woman to see me. She was taking amitriptyline, 25 mg three times daily, timolol and clonazepam. Four epidural corticosteroid injections had failed to alleviate the low back pain.

Perphenazine, 2 mg twice daily, was added to the regimen and markedly relieved the pain and stiffness; however, it had to be withdrawn because of akathisia. Lithium, 300 mg three times daily (resulting in a steady-state serum lithium level of 1.13 mmol/L), was substituted; it achieved virtually complete pain relief but produced unacceptable tremor. The dosing frequency was reduced to twice daily (resulting in a serum lithium level of 0.75 mmol/L); the woman experienced no tremor, but some pain and stiffness recurred. Attempts to increase the serum lithium level continued to result in tremor. Tenderness persisted on this regimen at numerous trigger points, but spontaneous pain and stiffness were greatly reduced.

Comments

Only one of the patients could not tolerate the optimum dose of lithium. All three patients experienced a prompt and marked reduction of pain and stiffness that was sustained; two enjoyed pain-free days for the first time since the onset of symptoms, and one had minimal pain 18 months after the lithium therapy was stopped. Laboratory tests showed no evidence of lithium toxicity to the thyroid or the kidney, and no goitres were noted. Trigger point tenderness was unchanged by the lithium therapy.

By definition fibromyalgia lacks both physical findings and objective criteria for response to treatment. Assessment of therapeutic efficacy is therefore entirely subjective and cannot be quantified. My long involvement with these patients, however, tends to substantiate their claims of marked and sustained improvement of their condition. None the less, these results need to be substantiated by further studies.

Augmentation therapy with lithium may be beneficial in fibromyalgia because it enhances the effect of TCAs on depression. Its success may also be due to unrecognized causes of fibromyalgia, such as hypomania, that are target symptoms for lithium and the phenothiazines. On the basis of the results described here I recommend that TCA therapy be augmented with lithium in resistant cases of fibromyalgia.

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Conferences

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May 22-25, 1991: North American Primary Care Research Group 19th Annual Meeting
Château Frontenac, Quebec
Abstract deadline is Dec. 14, 1990.
Dr. Michel Labrecque, chairman, Organizing Committee, NAPCRG-91, Continuing Medical Education Office, Faculty of Medicine, Ferdinand-Vandry Pavilion, Laval University, Quebec, PQ G1K 7P4; (418) 656-5958, FAX (418) 656-3442

May 23-24, 1991: 2nd Canadian Epidemiology Research Conference
University of Alberta, Edmonton
Dr. Colin Soskolne, conference convenor, 13-103 Clinical Sciences Bldg., University of Alberta, Edmonton, Alta. T6G 2G3; (403) 492-6013, FAX (403) 492-0364

May 26-29, 1991: 5th Canadian Congress of Rehabilitation — Science, Dignity, Opportunity
Prince Edward Hotel, Charlottetown
Congress Secretariat, Canadian Rehabilitation Council for the Disabled, 801-45 Sheppard Ave. E, Toronto, Ont. M2N 5W9; (416) 250-7490, FAX (416) 229-1371

May 27-29, 1991: 9th King's College International Conference on Death and Bereavement — Many Paths to Healing
London, Ont.
Dr. John D. Morgan, coordinator, Death Education Conference, King's College, 266 Epworth Ave., London, Ont. N6A 2M3; (519) 433-3491

May 30, 1991: Follow-up Workshop (in conjunction with the King's College International Conference) — The Psychology of Illness and the Art of Healing
London, Ont.
Dr. John D. Morgan, coordinator, Death Education Conference, King's College, 266 Epworth Ave., London, Ont. N6A 2M3; (519) 433-3491

May 30-June 1, 1991: International Conference on Stroke
Intercontinental Hotel, Geneva
Abstract deadline is Jan. 15, 1991.
Secretariat, International Conference on Stroke, c/o Kuoni Travel Ltd., 7 rue de Berne, CH-1211, Geneva 1, Switzerland; telephone 41-22-732-088, FAX 41-22-731-5078

June 2-5, 1991: Canadian Long Term Care Association Annual Conference
Halifax
Canadian Long Term Care Association, 302-260 St. Patrick St., Ottawa, Ont. K1N 5K5; (613) 237-9837, FAX (613) 237-6592

June 3-6, 1991: International Istanbul Symposium of Obstetrics and Gynecology
Atatürk Cultural Center, Istanbul
Dr. Necati Tolun, Cerrahpaşa Medical Faculty, Istanbul University, PO Box 12, Cerrahpaşa, Istanbul 34301, Turkey; telephone 011-90-1-586-15-14, FAX 011-90-1-588-48-85

June 19-22, 1991: 1st World Congress of Medical Polonia and 5th International Convention of the Polish Medical Association
Częstochowa, Poland
Official languages: Polish, English
Congress Office, Dr. Rydygier's Surgical Hospital, ul. Mirowska 25, 42 200 Częstochowa, Poland; telephone 011-48-34-477-13, 472-35, 414-15, 419-53 or 450-71, FAX 011-48-34-46-520

June 22-27, 1991: 16th World Congress of Anatomic and Clinical Pathology (sponsored by the World Association of Societies of Pathology and the Canadian Association of Pathologists)
Vancouver
WASP/CAP Secretariat, 645-375 Water St., Vancouver, BC V6B 5C6; (604) 681-5226, FAX (604) 681-2503

July 14-20, 1991: 1st World Congress on Wilderness Medicine (7th Annual Meeting of the Wilderness Medical Society and 1st in a series of quadrennial international events)
Chateau Whistler Resort, Whistler, BC
Abstract deadline is Apr. 1, 1991.
Dr. Douglas A. Gentile, Vanderbilt University, 243 Medical Center South, Nashville, TN 37212, (615) 343-4836; or Dian M. Simpkins, Wilderness Medical Society, PO Box 397, Point Reyes Station, CA 94956, (415) 663-9107